

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AFFYMETRIX, INC.)
Plaintiff,)
v.) C.A. No. 04-901 (JJF)
ILLUMINA, INC.,)
Defendant.)

**AFFYMETRIX'S OPPOSITION TO ILLUMINA'S MOTION TO VACATE AS A
MATTER OF LAW THE JURY'S VERDICT OF INFRINGEMENT OF THE '716
PATENT UNDER THE DOCTRINE OF EQUIVALENTS**

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SUMMARY OF ARGUMENT

While employed at Affymetrix, Dr. Mark Chee co-invented the '716 patent. Shortly after leaving Affymetrix, Dr. Chee founded Illumina. Fearing that assignor estoppel will prevent it from contesting the validity of the '716 patent, Illumina has made several attempts to remove the patent from this case. Earlier, Illumina filed a motion to dismiss the '716 patent on the ground that Affymetrix did not own the patent. The Court denied that motion. In its current Motion to Vacate the Jury's Verdict, Illumina once again seeks to escape the '716 patent which the Jury determined it infringed under the doctrine of equivalents. In doing so, Illumina argues a distorted view of the law and the prosecution history of the '716 patent. When those distortions are corrected, however, it is clear that Affymetrix did not surrender the equivalents found by the Jury to infringe, Illumina is without grounds to challenge the Jury's verdict, and Illumina's Motion should be denied.

As an initial matter, amendment-based prosecution history estoppel applies only to claim limitations that are actually amended during the prosecution. In this case, the Jury heard testimony that Illumina's technology infringed under the doctrine of equivalents based on a limitation that was **not** amended during prosecution. Therefore, Illumina has failed to establish the underlying predicate – establishing that the Jury found doctrine of equivalents infringement of an amended limitation – necessary even to begin the prosecution history estoppel analysis. For this reason alone, Illumina's motion should be denied.

Even if one looks beyond this threshold failure, Illumina's asserted alternative theories of prosecution history estoppel both fail. First, Illumina's claim of amendment-based estoppel misreads the Supreme Court's *Festo* decision in which the Court rejected the sort of mechanistic application of the doctrine that Illumina sets forth in its brief. *See Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722 (2002) ("Festo" or "Festo VIII"). In *Festo*

and its earlier decision in *Warner-Jenkinson Co. v. Hilton-Davis Chem. Co.*, 520 U.S. 17 (1997), the Supreme Court established a three-step analysis to ascertain whether an applicant surrendered a given equivalent as a matter of law through amendment. First, the amendment must have been a “narrowing” amendment – there must have been some claim scope surrendered by the change of language. *Festo*, 535 U.S. at 736. Second, under *Warner-Jenkinson*, 520 U.S. at 40-41, the amendment must have been made for a substantial reason related to patentability, *i.e.*, to overcome a rejection and obtain a patent. Then and only then does a presumption of surrender apply.

Finally, the “presumption” does not end the analysis. The Supreme Court set forth three independent ways in which a patentee can defeat the presumption of surrender depending on the nature of the equivalent and the amendment. First, “[t]he equivalent may have been unforeseeable at the time of the application.” *Festo*, 535 U.S. at 740-41. Second, “the rationale underlying the amendment may bear no more than a tangential relation to the equivalent in question.” *Id.* Third, “there may be some other reason suggesting that the patentee could not reasonably be expected to have described the insubstantial substitute in question.” *Id.*

The amendment Illumina asserts is at issue in this case (“indicating an extent of hybridization”) does not even get beyond the first step of the Supreme Court’s three-step analysis. Contrary to Illumina’s assertions of “amendment-based estoppel,” the amendment cited by Illumina was not a “narrowing amendment” that triggers the *Festo* presumption. Portions of the file wrapper ignored by Illumina make clear that the amendment was made in response to the Examiner’s suggestion that Affymetrix “clarify” whether the probe intensity in the claim was “an intrinsic property of each individual probe, or if the ‘intensity’ is actually a reflection of the extent of hybridization of probe molecules at a specific site on the chip.”

Therefore, the amendment was a clarifying – not a narrowing – amendment. Even if it could be viewed as a narrowing amendment, the amendment had at best a tangential relation to the actual equivalents found by the jury to infringe – the amendments were not made to overcome prior art, and the prior art that Illumina contends encompasses the infringing equivalents is in fact unrelated entirely. Under Supreme Court precedent, prosecution history estoppel does not apply for these two independent reasons.

Illumina’s case for “argument-based estoppel” fails for similar reasons. For an argument to create an estoppel of infringement by particular equivalents, there must have been a “clear and unmistakable surrender” of the equivalent. The prosecution history, however, shows that Affymetrix did not distinguish its invention from any technique using “tags” or “enzymes,” as Illumina suggests, but only from the fundamentally different sequencing technologies and image analysis systems disclosed in the Weiss and Stockham references at issue. The Examiner never contended that Weiss or Stockham disclosed the equivalent found to infringe by the Jury. Illumina’s arguments – similar to those it made unsuccessfully at trial – gloss over the substance of the applicant’s position, substituting a cursory word search of the file wrapper for the analysis that the law demands. Affymetrix no more surrendered any use of “tags” or “enzymes” in a sequencing assay than it did “DNA” or “molecules.” By precluding any use of any components used in a prior art reference, however minor, or concepts, however abstract, Illumina’s argument would vitiate the doctrine of equivalents.

By failing to address head-on the nature of Affymetrix’s amendments and the substance of the prior art, Illumina sidesteps the critical components of both the *Festo* inquiry and the analysis of the alleged “argument-based estoppel.” Illumina cannot shirk the Jury’s verdict so easily. The law does not allow it. Illumina’s Motion should be denied.

NATURE AND STAGE OF THE PROCEEDINGS

On February 8, 2007, the Court ordered that trial in this matter would be separated into several phases. The first phase, which was tried to a jury in March of 2007, included the issues of infringement and damages. As Illumina acknowledges, the Court barred evidence and argument relating to prosecution history estoppel from the phase I trial. (Illumina Br. at 11, n. 7). Despite the Court's ruling, however, Illumina pursued its "argument-based estoppel" position at trial. Indeed, Illumina's position in its brief neatly tracks Illumina's cross-examination of Affymetrix's expert Dr. Rudy Guerra and a line of direct questioning of Illumina's expert, Dr. John Quackenbush.

For example, Illumina's counsel asked Dr. Guerra if he had "reviewed the prosecution history of the '716 patent, this give and take back and forth to see how it might impact how these claims should be applied?" (Trial Tr. (Guerra) at 875:4-8). He then asked Dr. Guerra, "you would agree with me that during this give and take process, during this give and take process with the Patent Office that Affymetrix had to distinguish prior art that taught the use of both enzymes and tags; correct?" (Trial Tr. (Guerra) at 875:10-15). Later, on direct, Illumina's counsel asked Dr. Quackenbush to discuss the same Office Action and subsequent remarks by Affymetrix relied upon by Illumina here. (Trial Tr. (Quackenbush) at 1244:1-1248:20). Dr. Quackenbush offered his own interpretation to the Jury: "So Affymetrix is saying look, Weiss describes using an enzyme with tags, so they're saying here that, in fact, they're different, their invention is different than the Weiss invention which has these enzymes and tags." (Trial Tr. (Quackenbush) at 1245:23-1246:4).

Based on the expert's testimony, the jury found that the '716 was not infringed literally, but was infringed under the doctrine of equivalents. The jury also found that all of the asserted claims of the other four asserted patents were infringed. It awarded a 15% reasonable

royalty, with damages of \$16,727,459 having accumulated through 2005. Trial of the remaining issues will be discussed at the status conference set for October 10, 2007.

Prior to the phase I trial, on July 7, 2006, Affymetrix filed a Motion for Summary Adjudication on Illumina, Inc.'s Third and Seventh Affirmative Defenses, which seeks to preclude Illumina from contesting the validity of the '716 patent on the ground of assignor estoppel. That motion is still pending. Faced with the prospect of being unable to contest the validity of the infringed '716 patent, Illumina moved to dismiss the '716 patent from the lawsuit on the basis that Affymetrix did not own the patent. That motion was denied. Now, after having been found to infringe the patent (and still faced with the prospect of being unable to contest the validity of the infringed '716 patent), Illumina attempts to knock out the jury's infringement verdict with its motion to vacate (filed notwithstanding the parties' earlier agreement to withhold briefing of posttrial motions until a time prescribed by the Court. [D.I. 433].)

STATEMENT OF FACTS

I. ILLUMINA'S INFRINGING EQUIVALENTS

The asserted claims of the '716 patent are directed to "a computer program product" (or "a system") "that identifies an unknown base in a sample sequence." (DTX 3, '716 Patent, col. 41, ll. 60-62). All of the asserted claims require

computer code that receives a plurality of signals corresponding to probe intensities for a plurality of nucleic acid probes, each probe intensity indicating the extent of hybridization of a nucleic acid probe with at least one nucleic acid sequence including said sample sequence, and each nucleic acid probe differing from each other by at least a single base.

('716 Patent, col. 41, ln. 63-col. 42, ln. 60). At trial, Affymetrix's expert, Dr. Guerra, testified that all elements of each asserted claim are met literally by Illumina's GoldenGate and Infinium assays, and GenCall software. (Trial Tr. (Guerra) at 786:21-787:4). Dr. Guerra also offered

contingent arguments that, in the event aspects of Illumina's GoldenGate and Infinium assays were found to lie outside the literal scope of the claims, they were infringing equivalents.¹ (*Id.* at 809:14-811:16; 821:17-822:19). At the end of the trial, the Jury found that Illumina's assays and software infringed claims 1, 5 and 9 of the '716 patent under the doctrine of equivalents.

II. THE PROSECUTION HISTORY OF THE '716 PATENT

The application leading to the '716 patent was filed on October 21, 1994. (DTX4 at IAFP00000182). The patent issued on August 18, 1998. (*Id.*). Illumina's motion focuses on an Office Action of December 19, 1995, and the applicant's corresponding amendment and remarks.

Prior to that amendment, pending claim 1 of the application read:

1. In a computer system, a method of identifying an unknown base in a sample nucleic acid sequence, said method comprising the steps of:

inputting a plurality of probe intensities, each of said probe intensities being associated with a nucleic acid probe on a chip;

said computer system comparing said plurality of probe intensities wherein each of said plurality of probe intensities is substantially proportional to said associated probe hybridizing with at least one nucleic acid sequence, said at least one nucleic acid sequence including said sample sequence;

calling said unknown base according to results of said comparing step.

¹ Illumina's brief is cryptic with regard to what aspect of its assays it contends Affymetrix surrendered, instead referring to "the alleged equivalent." The Jury found Illumina's assays to be infringing equivalents when used with Illumina's data analysis software. Illumina never identifies what aspect of those assays it contends Affymetrix surrendered, however, other than referring vaguely to "enzyme-based assays" or "enzymes and tags." This failure to articulate the specific equivalents is further evidence that Illumina is unable to match what was allegedly surrendered to what was found to be an infringing equivalent by the Jury.

(DTX 4 at IAFP00000350-51 (October 17, 1995 amendment)).

The Examiner rejected claim 1 on grounds of indefiniteness, stating that the claims needed clarification:

Claim 1 is indefinite in reciting ‘probe intensities being associated with a nucleic acid probe on a chip’ in that *it is not clear* how the probe intensity is ‘associated’ with the probe. For example, *it is not clear* whether an ‘intensity’ is an intrinsic property of each individual probe, or if the ‘intensity’ is actually a reflection of the extent of hybridization of probe molecules at a specific site on the chip. *The claim might be amended to clarify this point.*

(*Id.* at IAFP00000366 (Office Action of December 19, 1995) (emphasis added)).

The Examiner also rejected the original claims as obvious in light of WO 92/10588, filed by Fodor, et al. (“Fodor”), in view of Weiss *et al.*, U.S. Patent No. 5,470,710 (“Weiss”) and Stockham *et al.*, U.S. Patent No. 5,273,632 (“Stockham”). (*Id.* at IAFP00000371). The Examiner cited Weiss and Stockham *not* for the assays used to generate data for programs claimed in those references, but for the *data analysis algorithms* they described. (*Id.* at IAFP00000371-74). The Examiner said that Fodor taught a method of “sequencing by hybridization” (“SBH”) involving overlapping of subsequences obtained from a microarray, but did not utilize the comparison of intensities to determine the identity of a base.

Fodor . . . teaches an SBH method wherein initial data resulting from a detection system is an array of data indicative of fluorescent intensity versus location of a substrate. . . The method of Fodor et al. differs from that of the present invention in that intensity ratios are not compared as a means on [sic] determining the identity of a base, rather it is the location of the signal which is called. . . .

(*Id.* at IAFP00000371-72).

The Examiner argued that Weiss and Stockham both involved calculation of intensity ratios. (*Id.* at IAFP00000372-74). According to the Examiner, Weiss teaches “that a CCD snapshot of hybridization signals may be obtained and pixel values may be determined and

averaged. . . . Ratios of signal intensities are determined using this system, and statistics used to calculate standard deviations of sample intensities versus background signals.” (*Id.* at IAFP00000372). Stockham “teaches a method of computerized analysis of the visual images of DNA sequence ladders” that also involved “a comparison of the ratios of intensities at a segment of a lane.” (*Id.* at IAFP00000372-73). The Examiner stated that:

The methods of Weiss and Stockham do not set any limits on the numbers of ratios that can be determined using their computer system. Therefore it would have been *prima facie* obvious to one of ordinary skill in the art at the time that the invention was made *to use the computer algorithms of Stockham and Weiss to interpret the data from the SBH system of Fodor*, given that one could ‘call’ a site based on the intensity of a signal produced by an associated probe at that site and thus assign an identity to that site.

(*Id.* at IAFP00000373 (emphasis added)).

Affymetrix canceled the original claims and submitted new claims. Cancelled claim 1 corresponded to new claim 60, which required:

inputting a plurality of probe intensities for a plurality of nucleic acid probes, each probe intensity indicating an extent of hybridization of a nucleic acid probe with at least one nucleic acid sequence including said sample sequence, and each nucleic acid probe differing from each other by a single base.

(*Id.* at IAFP00000390-91 (May 20, 1996 Amendment)). In its remarks, Affymetrix noted that:

In regard to claim 1, the Examiner stated that it is *not clear* how a probe intensity is associated with a nucleic acid probe. *As the Examiner suggested, applicants amended claim 60* to recite ‘each probe intensity indicat[es] an extent of hybridization with a nucleic acid probe with at least one nucleic acid sequence including said sample sequence.’ Accordingly, the rejection does not apply to the new claims.

(*Id.* at IAFP00000399 (emphasis added)).

Affymetrix also addressed the Examiner’s rejection under § 103 in light of Fodor – also assigned to Affymetrix – in view of Weiss and Stockham, noting that “Fodor describes,

among other things, pioneering techniques for sequencing by hybridization. However, the examiner cited Weiss and Stockham for disclosing the base calling (identifying) methods of the present invention. . . . [T]hese references do not disclose or suggest the invention as claimed.” (*Id.* at IAFP00000401-402).

As Affymetrix explained, both Weiss and Stockham are directed toward a method of sequencing very different from the base calling techniques disclosed in the ‘716 patent. (*Id.* at IAFP00000402 (“Weiss and Stockham are related to nucleic acid sequencing which utilizes nucleic acid ladders which may be formed by well known techniques such as the Sanger dideoxy method or the Maxam and Gilbert method.”)). Stockham explains the principles behind sequencing using nucleic acid ladders. (*See* Stockham at col. 1, ll. 46-62). These methods allow sequencing by generating a series of sequence fragments that differ in length by a single base. These fragments are then allowed to migrate across a gel matrix upon application of an electric field (“electrophoresis”) under conditions where migration rate is determined by the size of the fragment, *i.e.*, the number of nucleotides. (*See id.*). Because the chemical reactions used to generate the fragments generate fragments for which the nucleotide at the end of the fragment can be determined, the result is a “ladder” of fragments differing in size by a single base and ending with a known base. (*See id.*). These “sequence ladders” can be visualized and “read” and sequence assembled from these data. (*See id.* at col. 1, ln. 66-col. 2, ln. 4).

Affymetrix then explained the particular variations of these techniques described in Weiss and Stockham:

More specifically, Weiss describes utilizing an enzyme on identical probes that hybridize with tags in the fragments of the nucleic acid ladder. The enzymes convert a fluorogenic substrate (e.g., BBTP) into a fluorescent product in order to enhance the pattern of hybridization.

Stockham, more specifically, describes methods of sharpening signal peaks from electrophoretic migration patterns of nucleic acid ladders. . . .

(DTX 4 at IAFP00000402).

Affymetrix observed that neither Weiss nor Stockham describes any of *three* limitations of claim 1: “inputting a plurality of probe intensities,” “each probe intensity indicating an extent of hybridization of a nucleic acid probe,” or “each nucleic acid differing from each other by a single base.” (*Id.*).

With regard to Weiss, Affymetrix stated that:

Weiss uses a single probe which will hybridize to a tag on the nucleic acid ladder fragments. As such, all of the “probes” in Weiss are identical. Furthermore, the probes in Weiss do not indicate an extent of hybridization but instead are utilized to generate a fluorescent signal which indicates the location of a fragment on the substrate. Accordingly, it is the location of the fragments that is used to sequence a nucleic acid.

(*Id.* at IAFP00000402-403). With regard to Stockham:

Stockham does not utilize probes at all. Instead, Stockham recites that the fragments of the nucleic acid ladder are radioactively labeled. The radioactive signal resulting indicates the position of the fragments on the gel in a way which is similar to Weiss. Accordingly, Stockham also utilizes the location of the fragments to sequence a nucleic acid.

In stark contrast, the present invention compares probe intensities that indicate the extent of hybridization of probes differing by a single base and the sample nucleic acid sequence.

(*Id.* at IAFP00000403).

Affymetrix argued that the algorithms of Weiss and Stockham were inapplicable to array-based technologies because algorithms for analyzing nucleic acid ladders were “vastly different technologies”:

Weiss and Stockham relate to vastly different technologies than the pioneering advances of Fodor. Weiss and Stockham are directed

to identifying the location of a fragment of a nucleic acid ladder. In the present invention, the locations of the hybridized probes are known and, as such, the computer algorithms of Weiss and Stockham would indeed seem to teach away from the present invention which is directed to calling an unknown base according to probe intensities from nucleic acid probes that differ by a single base.

(*Id.* (emphasis in original)).

As such, Affymetrix distinguished the Weiss and Stockham references based on the “vastly different” sequencing technologies to which the algorithms disclosed in those references pertained. Importantly, Affymetrix did *not* distinguish Weiss and Stockham on the basis of the general use of “tags” or “enzymes.”

ARGUMENT

I. STANDARD OF REVIEW

Whether prosecution history estoppel applies to limit the doctrine of equivalents is a question of law for the Court. *See Bai v. L & L Wings, Inc.*, 160 F.3d 1350, 1354 (Fed. Cir. 1998). Similarly, the scope of any surrender under the doctrine of equivalents is also a question of law. *K-2 Corp. v. Salomon S.A.*, 191 F.3d 1356, 1359 (Fed. Cir. 1999).

II. AMENDMENT-BASED ESTOPPEL DOES NOT APPLY

A. Illumina Has Failed To Satisfy The Threshold Requirement That The Jury Found Doctrine Of Equivalents Infringement Of An Amended Limitation

It is axiomatic that amendment-based estoppel operates to preclude a finding of infringement under the doctrine of equivalents *only* of limitations that were actually amended during the prosecution, assuming all of the other requirements are met. *Biagro W. Sales, Inc. v. Grow More, Inc.*, 423 F.3d 1296, 1305 (Fed. Cir. 2005) (“If the narrowing amendment was the addition of a new claim limitation, as in the case before us, equivalents are presumptively not

available with respect *to that limitation.*") (emphasis added). In this case, the jury heard testimony that Illumina infringed under the doctrine of equivalents based on a limitation that was *not* amended during prosecution. Therefore, Illumina's motion fails to meet this threshold requirement – establishing that the jury actually found doctrine of equivalents infringement of an amended limitation – and must be denied.

In connection with the claim construction in this case, the parties asked the Court to construe a number of limitations of the '716 patent claims, including "probe intensity" and "indicating an extent of hybridization." The Court defined "probe intensity" in the claims of the '716 patent to mean "intensity from a labeled sample nucleic acid hybridized to a probe location." [D.I. 325] As set forth in Illumina's motion (Illumina Br. at 8-9), Dr. Guerra, Affymetrix's '716 infringement expert, testified that the "probe intensity" limitation was met under the doctrine of equivalents by Illumina's technology. For example, with regard to the Infinium assay, Dr. Guerra testified that the fact that the probe intensity was recorded after the patient DNA had been removed was, at most, an insubstantial difference under the doctrine of equivalents:

There might be *some question as to whether the intensity that is read off from this particular probe A while the patient DNA is not hybridized at the time that the scanning is done*, that is really irrelevant because the double-stranded hybrid is done at the probe location. The fact that it has been removed does not in any way affect the biotin labeling. It doesn't affect the fluorescent labeling and it doesn't affect the intensity reading, and so in the end, we end up getting an intensity reading by a labeled sample nucleic acid at a probe location.

(Trial Tr. (Guerra) at 810:5-17 (emphasis added)). This testimony related to the "probe intensity" limitation – Dr. Guerra was explaining that intensity generated from the Infinium probe was the equivalent to intensity generated from a "labeled sample" as required by the Court's construction.

Similarly, Dr. Guerra testified with respect to the GoldenGate assay that the “hybridized to a probe location” portion of the Court’s construction of “probe intensity” was met under the doctrine of equivalents:

It’s largely the same idea as before in that *there might be some question as to this notion of hybridizing to a probe location*. The hybridization actually occurs in solution as indicated by this day one workflow. And it’s not until we get to this amplicon stage that these amplicons then get exposed to the array and then they go to the probe location.

However, as I said before, whether this particular patient DNA gets sent to the bead or not, it’s not really relevant here because we have the amplicon which has that particular fragment, that black part that is identical to the patient DNA, except it’s just complementary.

So if I want to know about the signal intensity of the patient DNA at a particular location, that’s the same as getting the intensity from the amplicon through the complimentary base rule.

(Trial Tr. (Guerra) at 821:17-822:19 (emphasis added)). The “probe intensity” limitation, however, was not itself amended – it appeared in the claim prior to the amendment (DTX 4 at IAFP00000350-51) and afterwards. It should not be the basis for an amendment-based estoppel.

Illumina relies on the new limitation added to the claims – “indicating an extent of hybridization” to support its amendment-based estoppel argument. Dr. Guerra testified that this limitation was met literally, and there is no evidence that the jury found it was not met literally. (Trial Tr. (Guerra) at 808:19-809:9; 820:15-18). Thus, the premise of Illumina’s motion – that the jury necessarily found doctrine of equivalents infringement of an amended limitation – is incorrect and it motion should be denied.

B. Affymetrix Did Not Surrender The Claimed Equivalents When Amending The Claims To Clarify The Nature Of The Invention

The Supreme Court clarified the nature of the prosecution history estoppel inquiry in *Festo*, 535 U.S. at 733-41. By its holding, the Supreme Court rejected the “complete bar” rule put forward by the Federal Circuit. *See id.* at 737. Under the discredited “complete bar” rule, an amendment made during prosecution that (1) narrowed the scope of a claim (2) for any “substantial reason related to patentability” barred any application of the doctrine of equivalents with regard to that element. *Id.* Observing that the Federal Circuit’s rigid “complete bar rule” contradicted governing Supreme Court and Federal Circuit precedent, the Supreme Court rejected the “complete bar” rule outright. *Id.* According to the Supreme Court, only equivalents **surrendered by the patentee** when amending the claims are barred:

Though prosecution history estoppel can bar a patentee from challenging a wide range of alleged equivalents made or distributed by competitors, **its reach requires an examination of the subject matter surrendered by the narrowing amendment.** The complete bar avoids this inquiry by establishing a *per se* rule; but that approach is inconsistent with the purpose of applying the estoppel in the first place—to hold the inventor to the representations made during the application process and to the inferences that may reasonably be drawn from the amendment. By amending the application, the inventor is deemed to concede that the patent does not extend as far as the original claim. It does not follow, however, that the amended claim becomes so perfect in its description that no one could devise an equivalent. After amendment, as before, language remains an imperfect fit for invention.

Id. at 737-38 (emphasis added). Thus, a limitation that has been added or amended may be infringed under the doctrine of equivalents, and the patentee is estopped only from claiming that subject matter surrendered to obtain a patent may serve as an infringing equivalent.

A three-part inquiry flows from *Festo* and *Warner-Jenkinson* as described by the Federal Circuit, *en banc*, on remand from the Supreme Court’s *Festo* decision. *Festo Corp. v.*

Shoketsu Kinzoku Kogyo Kabushiki Co., 344 F.3d 1359, 1366-67 (Fed. Cir. 2003) (“*Festo IX*”).

First, only a narrowing amendment may trigger an estoppel. *See id.* at 1366. Not all additions or alterations of claim language actually work an estoppel – only those that change the scope of the claim. Second, a narrowing amendment must have been made for a “substantial reason related to patentability” – the amendment must have been made to overcome a rejection and to obtain a patent. *Id.* at 1366-67.

Third, if the narrowing amendment was made for a substantial reason related to patentability, the patentee has the opportunity to rebut the presumption of an estoppel and demonstrate that particular equivalents are not within the scope of subject matter surrendered. *Id.* at 1367. As the Supreme Court stated, there is no reason “to foreclose claims of equivalence for aspects of the invention that have only a peripheral relation to the reason the amendment was submitted.” *Festo*, 535 U.S. at 1841. That a claim was amended “shows only that [the patentee] was familiar with the broader text” upon which a rejection was based “and with the difference between” the claimed invention and prior art. *Id.* “As a result, there is no more reason for holding the patentee to the literal terms of an amended claim than there is for abolishing the doctrine of equivalents altogether and holding every patentee to the literal terms of the patent.”

Id.

1. Affymetrix’s Amendments Did Not Narrow The Scope Of The Claims

Not every amendment to a claim changes the scope of that claim. In cases in which the amendment does not narrow the claim, it follows that the *Festo* presumption of surrender is inapplicable. *See Honeywell Int’l v. Hamilton Sundstrand Corp.*, 378 F. Supp. 2d 459, 476 (D. Del. 2005). Here, the amendment relied upon by Illumina was added pursuant to

the examiner's request to *clarify* the meaning of the claim, rather than to avoid a prior art rejection. It was not a "narrowing amendment" that would preclude equivalents.

Prior to the Examiner's Office Action, claim 1 required "probe intensities being associated with a nucleic acid probe on a chip." (DTX 4 at IAFP00000350-51 (October 17, 1995 amendment)). The Examiner rejected claim 1 as indefinite because, in her view, the "association" between the probe and probe intensity was unclear: "***it is not clear*** whether an 'intensity' is an intrinsic property of each individual probe or if the 'intensity' is actually a reflection of the extent of hybridization of probe molecules at a specific site on the chip. ***The claim might be amended to clarify this point.***" (*Id.* at IAFP00000366 (Office Action of December 19, 1995)). The Examiner was requesting clarification – not suggesting that the scope of the claim encompassed unpatentable subject matter.

The specification and language of the claim prior to amendment demonstrate that the probe intensities were associated with the hybridization of a probe and a sample. The "Summary of the Invention" states that the claimed computer system "provides, among other things, improved methods of analyzing fluorescent image files of chip containing ***hybridized nucleic acid probes.***" (*Id.* at IAFP00000191, ll. 24-26 (application) (emphasis added)). Moreover, the claim *already* required that "each of the probe intensities is substantially proportional to a probe hybridizing to at least one sequence" This proportionality is the relationship that the Examiner wanted clarified – the intensity is proportional to the extent to which the probe and sample were hybridized. (*Id.* at IAFP00000350-51 (October 17, 1995 amendment)).

No reading of the specification would suggest that a probe intensity would be an inherent property of the probe. As suggested by the Examiner, however, this is clarified and

made explicit by the amendment. Indeed, upon amending the claims, Affymetrix said as much, indicating that the amendment was made “[a]s the examiner suggested.” (*Id.* at IAFP00000399).

A similar situation occurred in *Honeywell Int'l.*, 378 F. Supp. 2d at 471-77. In *Honeywell*, the Court found that a patentee was not estopped from asserting infringement by equivalents to an amended limitation where the amendments had not changed claim scope. *Id.* Finding that patentee Honeywell had amended the claims for purposes of clarification, the Court recognized that “an amendment to a claim limitation is not necessarily narrowing, even when a side-by-side comparison makes it appear to be.” *Id.* at 474. The Court found that the scope of the claim had not been narrowed, reasoning that its holding was in keeping with the Supreme Court’s *Festo* decision:

Given the inability of language to always fully “capture the essence of a thing in a patent application,” *id.* at 731, 122 S.Ct. 1831, it is often very difficult to discern whether an amendment is merely an alternative way of describing the same thing, or whether it actually surrenders subject matter. Thus, it would be inaccurate and imprudent to conclude that an amendment narrows the scope of a claim by merely giving the original and amended limitations a cursory, side-by-side comparison, without first exploring the entire prosecution history.

Id. at 476-77. Because the claim had not been narrowed, prosecution history estoppel did not apply. *Id.*

As the Court noted in *Honeywell*, the Federal Circuit reached similar conclusions in two pre-*Festo* cases, *Interactive Pictures Corp. v. Infinite Pictures, Inc.*, 274 F.3d 1371 (Fed. Cir. 2001) and *TurboCare Div. Of Demag Delaval Turbomachinery Corp. v. General Electric Co.*, 264 F.3d 1111 (Fed. Cir. 2001). In *Interactive Pictures*, the Federal Circuit found that amendment of a limitation from “output signals” to “output transform calculation signals” did not change the meaning of the claim. *Id.* at 1377. (“As to the amendment-based estoppel issue, we conclude that the addition of the words ‘transform calculation’ was not a narrowing

amendment because that addition did nothing more than make express what had been implicit in the claim as originally worded. That interpretation flows from the original claim as a whole and in light of the specification.”) Similarly, in *TurboCare*, 264 F.3d at 1125, decided prior to the Supreme Court’s rejection of the complete bar rule, the Federal Circuit held that the addition of a limitation defining the diameter of a “small clearance position” to require “contact” between different surfaces was not a narrowing amendment because the specification made clear that the small diameter position was so defined before the amendment. *Id.* (“Here, the newly added claim only redefined the small clearance position limitation without narrowing the claim. Therefore *Festo* is not applicable.”) (citing *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 234 F.3d 558 (Fed. Cir. 2000) (*en banc*), vacated, 535 U.S. 722 (2002)). *Id.* at 1126. For the same reason, Affymetrix’s amendment is not a narrowing amendment – it simply made clear what was already so defined in the specification and the claim, namely that the “probe intensities” indicated an extent of hybridization.

That Affymetrix referred to the claims “as amended” when explaining why the data analysis programs disclosed in Weiss and Stockham did not render the claimed invention obvious also does not suggest any narrowing of scope. It is not surprising that Affymetrix would refer to its new claims or added limitations when overcoming prior art if the older claims had already been cancelled because they were not as clear. As discussed in more detail below, the gravamen of Affymetrix’s arguments to overcome Weiss and Stockham was that these references generated sequence from “sequencing ladders” visualized using probes that were identical – acting essentially to visualize the fragments in the ladder – or no probes at all. By contrast, Affymetrix’s invention analyzed data from an array of sequences – making base calls from probe

intensities reflecting hybridization differences between probes differing by a single base. These aspects of the invention were always there – not added to overcome any rejection.

Additionally, Affymetrix certainly did not concede that it needed to amend the claim to overcome Weiss and Stockham. Among the limitations that Affymetrix argued were not present in Weiss or Stockham was “inputting a *plurality* of probe intensities.” (DTX 4 at IAFP00000402 (May 20, 1996 Amendment) (emphasis added)). Affymetrix argued that Weiss utilized “identical” probes, and Stockham no probes at all. (*Id.* at IAFP00000402-403). As such, there was no need for Affymetrix to add an additional limitation to overcome this prior art. The limitation was added only to make clear the scope of the invention, and, as a result, was not a narrowing amendment.

2. Even If Affymetrix’s Amendment Were Found To Have Narrowed Claim Scope, Affymetrix Did Not Surrender The Infringing Equivalents

Even if the amendment relied upon by Illumina had narrowed the claims, and had been made for a substantial reason relating to patentability, Affymetrix can rebut the presumption of surrender of the full scope of equivalents.² *See Insituform Techs., Inc. v. CAT Contracting, Inc.*, 385 F. 3d 1360, 1367 (Fed. Cir. 2004). In this case, the equivalent found by the Jury to infringe the ‘716 patent was, at best, tangential to the rationale underlying the amendment. *See id.*

² Curiously, although in parts of its brief Illumina acknowledges that a patentee can rebut the *Festo* presumption, it also states that “Affymetrix narrowed its claims in response to a rejection, and the presumption of estoppel is invoked. As a result, Affymetrix is estopped from asserting infringement based on equivalents of the narrowed claim, and the jury’s finding of infringement of the ‘716 patent under the Doctrine of Equivalents must be vacated.” (Illumina Br. at 14). Of course, Illumina is wrong – another condition applies. A “presumption” becomes an estoppel only if Affymetrix cannot rebut the presumption – and as much as Illumina would like to dispose of Affymetrix’s rebuttal in a conclusory and dismissive fashion, it cannot.

A patentee can rebut the *Festo* presumption by showing that “the reason for the narrowing amendment was peripheral, or not directly relevant, to the alleged equivalent.” *Festo IX*, 344 F.3d 1359, 1369 (quoting *Festo*, 535 U.S. at 740). The reason for the amendment is objectively demonstrated within the prosecution history. *Festo IX*, 344 F.3d at 1369 (“[T]he inquiry into whether a patentee can rebut the *Festo* presumption under the ‘tangential’ criterion focuses on the patentee’s objectively apparent reason for the narrowing amendment. As we have held in the *Warner-Jenkinson* context, that reason should be discernible from the prosecution history record, if the public notice function of a patent and its prosecution history is to have significance.”)

An equivalent is tangential if the prosecution history shows that it is not within the scope surrendered, given the reason for the amendment. *See Primos, Inc. v. Hunter’s Specialties, Inc.*, 451 F.3d 841, 849 (Fed. Cir. 2006). In *Primos*, the court found that an amendment adding a requirement that two plates be “differentially spaced” surrendered equivalents in which the plates were *not* “differentially spaced,” as in the prior art that formed the basis of the rejection, but that the rationale behind the amendment was tangential to the accused equivalent, which featured a dome-shaped structure, rather than a flat plate:

We agree with the district court . . . that the territory surrendered by the ‘differentially spaced’ amendment comprises plates that are not differentially spaced above the membrane. That conclusion is consistent with the prosecution history. The patentee added the “differentially spaced” limitation to distinguish the diaphragm mouth call from a prior art device that consisted of a shelf-like structure positioned on top of the membrane without any spacing. The accused device, however, includes a dome that is spaced above the membrane. Because the accused device’s dome includes the spacing, the amendment was merely tangential to the contested element in the accused device, and thus prosecution history estoppel does not apply to prevent the application of the doctrine of equivalents.

Id.

Illumina contends that Affymetrix's addition of a limitation requiring that probe intensities "indicate an extent of hybridization" estops Affymetrix from asserting infringement under the doctrine of equivalents of enzyme- and tag-based assays. (Illumina Br. at 15 ('Because the amendment was made in part to distinguish prior art relating to enzymes and tags . . . it is anything but tangential to the adjudged equivalent.')). What Illumina does not address, however, is that the rationale underlying the amendment bears, at most, a tangential relation to these equivalents. Put simply, the reason for the amendment, even if one views it as narrowing, had very little to do with enzymes and tags.

As explained below with regard to Illumina's assertion of "argument-based estoppel," Illumina misreads the prosecution history to suggest that Affymetrix amended claims to avoid the use of "enzymes and tags" in hybridization-based assays. As an initial matter, Affymetrix's mention of enzymes and tags in the prosecution history is *not* tantamount to a suggestion that they serve as points of distinction between the prior art and Affymetrix's hybridization-based assays.³ The prosecution history indicates that Affymetrix distinguished Weiss and Stockham based not on the general use of "enzymes and tags" in those references, but rather due to the references' utilization of image analysis software to analyze sequencing ladders, rather than arrays. (DTX 4, IAFP00000401-404 (May 20, 1996 Amendment)). As Affymetrix indicated to the Examiner, analysis of sequencing ladders involves determination of the relative locations of fragments in two-dimensional space, such that relative location communicates

³ Illumina suggests that an amendment made to overcome prior art containing the alleged equivalent is *per se* not tangential. (Illumina Br. at 15). Setting aside the fact that the prosecution history contains no indication that the claim was amended to overcome the prior art, Illumina does not and cannot show that its array-based assays are encompassed within the Weiss and Stockham prior art directed toward sequencing techniques involving ladders. They are fundamentally different technologies and, therefore, any distinguishing of Weiss and Stockham does not preclude claim coverage of Illumina's assays.

sequence information. (See *id.* at IAFP00000403). “In stark contrast,” Affymetrix’s invention took as an input intensity from specific locations correlated to different probe sequences. (*Id.*). The fact that enzymes or tags are used to generate the sequence ladders in Weiss (or enzymes only, in Stockham) is tangential to Affymetrix’s arguments, at best.

As a matter of logic and law, *any* use of enzymes or tags would not be foreclosed simply because an applicant distinguished a reference that employs these ubiquitous biological reagents to very different ends than the infringing equivalent. As one of skill in the art would understand, “enzymes” and “tags” are extremely common in molecular biology.⁴ Virtually any manipulation in molecular biology will utilize enzymes. Affymetrix no more distinguished the use of “enzymes” or “tags” than it did “DNA.” By identifying commonly used elements within the prior art and abstracting from those elements beyond recognition, Illumina argues that Affymetrix distinguished *all* assays using enzymes or tags. By the same logic, Affymetrix would be barred from claiming equivalents utilizing DNA or involving sequencing, an obviously absurd position.

The Federal Circuit held that a patentee successfully rebutted the *Festo* presumption where an amendment was tangential to an infringing equivalent in *Insituform*

⁴ During the trial, Illumina repeatedly suggested that Affymetrix’s assays did not use enzymes and tags. The evidence showed otherwise. For example, Dr. Stephen Fodor, Affymetrix’s founder and CEO, testified that “[t]here are products that use enzymes to distinguish matches and mismatches.” (Trial Tr. (Fodor) at 384:7-9; *see also* Trial Tr. (Fodor) at 286:15 (discussing Affymetrix “TagArray”)). Dr. David Barker, Illumina’s former Chief Scientific Officer, after first claiming that an Affymetrix paper did *not* discuss the use of enzymes to call bases, later had to concede that it did:

Q. They’re using enzymology, aren’t they? Is that a yes?

A. Yes, that’s correct. Not the same as the GoldenGate assay, but that’s correct.

(Trial Tr. (Barker) at 1134:5-9).

Techs., Inc. v. CAT Contracting, Inc., 385 F.3d 1360, 1368 (Fed. Cir. 2004). The patentee invented a process for patching holes in pipes “in situ,” *i.e.*, while the pipes remained in the ground. *Id.* at 1362. The claim at issue claimed a process for impregnating the interior of a flexible tube with resin by creating a vacuum within the tube. *Id.* at 1362-63. The claimed process involved making a hole in the tube and applying a single cup attached to a vacuum source over the hole. *Id.* at 1368. The original claims did not restrict the placement of the vacuum source or the number of cups. *Id.* at 1368-69. The defendant’s process used multiple cups. *Id.* at 1368. The defendant contended that, because the single cup limitation had been added during prosecution to overcome a prior art rejection, the patentee was foreclosed from asserting infringement by a device utilizing more than one cup under the doctrine of equivalents.

Id.

The Federal Circuit held that the patentee had rebutted the *Festo* presumption because the amendment was tangential to the equivalent in question, holding that “the amendment limiting the literal scope of claim 1 to a single cup process bears ‘only a tangential relation,’ if that, ‘to the equivalent in question,’ a process using multiple cups”:

The question we must address is “whether the reason for the narrowing amendment was peripheral, or not directly relevant, to the alleged equivalent.” . . . As the discussion above indicates, the narrowing amendment in this case was for the purpose of distinguishing the invention over Everson. Insituform made it clear that the difference between its process and Everson was that its process did not have the disadvantage of the Everson process of a large compressor at the end of the liner. There is no indication in the prosecution history of any relationship between the narrowing amendment and a multiple cup process . . .

Id. at 1370.

Similarly, here, Affymetrix’s stated purpose for its amendment was to clarify the association between probes and probe intensities, and communicate that probe intensities

reflected the extent of hybridization of a probe and sample (as do those used in Illumina's assays.) Neither Weiss nor Stockham bears any substantial relationship to Illumina's assays. Illumina's efforts to manufacture such a relationship by abstracting beyond recognition cannot serve to create such a relationship. Affymetrix distinguished Weiss and Stockham not on the basis of their general use of "tags" or "enzymes" but, rather, because they utilized algorithms designed to analyze sequencing ladders, and not arrays.

In sum, even if Affymetrix did surrender some claim scope by its amendment, Illumina's equivalents were not within the scope surrendered.

III. ARGUMENT-BASED ESTOPPEL DOES NOT APPLY

Illumina's "alternative ground" in support of its motion, "argument-based estoppel," fares no better than its suggestion of "amendment-based estoppel." As Illumina acknowledges, argument-based estoppel requires "a clear and unmistakable surrender" of the infringing equivalents by the patentee. *AquaTex Indus., Inc. v. Techniche Solutions*, 419 F.3d 1374, 1382 (Fed. Cir. 2005) ("To invoke argument-based estoppel, the prosecution history 'must evince a clear and unmistakable surrender of subject matter.'") (quoting *Pharmacia & Upjohn Co. v. Mylan Pharm., Inc.*, 170 F.3d 1373, 1377 (Fed. Cir. 1999)). Apart from conclusory assertions that Affymetrix surrendered Illumina's infringing equivalents, Illumina cannot explain exactly how Affymetrix's arguments to the Examiner about the different sequencing technologies of Weiss and Stockham somehow signal any sort of a surrender of Illumina's assays, let alone a "clear and unmistakable" surrender.

Whether an argument creates an estoppel is an objective inquiry. *See AquaTex*, 419 F.3d at 1382 ("To determine if subject matter has been relinquished, an objective test is applied, inquiring 'whether a competitor would reasonably believe that the applicant had

surrendered the relevant subject matter.””) (quoting *Cybor Corp. v. FAS Techs., Inc.*, 138 F.3d 1448, 1457 (Fed. Cir. 1998)). The “surrender” must be “clear and unmistakable.” *See Aquatex*, 419 F.3d at 1382. Additionally, the arguments made by the patentee during prosecution must be viewed in context – not simply taken in isolation. *See Read Corp. v. Portec, Inc.*, 970 F.2d 816, 824 (Fed. Cir. 1992). For example, where a patentee distinguishes a prior art reference on several grounds, it does not create a separate estoppel for each aspect of the prior art forming a basis for distinction:

Every statement made by a patentee during prosecution to distinguish a prior art reference does not create a *separate* estoppel. Arguments must be viewed in context. In context, Read distinguished, for example, the Deister reference because of a wealth of differences. The Deister reference discloses a small screening device which has wheels as tall as the device itself

Read pointed out differences not only respecting the wheels, including that they were not collapsible and were in a different location (on the side, not the end) but also marked differences in *other* parts of the structure. Thus, any estoppel created by Portec's argument encompasses *all* of these *combined* distinctions of Deister and not an estoppel respecting *each* of the *individual* differences, *e.g.*, that any device with non-movable wheels cannot infringe.

Id. (emphasis in original).

Similarly, in *Aquatex*, 419 F.3d at 1382, the Federal Circuit reversed a trial court's determination that prosecution history estoppel barred application of the doctrine of equivalents against an infringer where the trial court failed to appreciate the nature of the patentee's argument in context. The patentee and alleged infringer manufactured clothing that cooled the wearer through evaporation, and the asserted patent claimed a method for cooling a person that included the limitation “providing a multi-layered, liquid-retaining composite material comprising a fiberfill batting” material. *Id.* at 1377. The claims were construed to require synthetic fiberfill. *See id.* at 1382. During prosecution, the patentee had argued that a

prior art reference, the “‘297 patent,” “fails to disclose or suggest the fiberfill batting and polymeric fibers and/or particles of the composite material in the claimed method.” *Id.* at 1383. The trial court interpreted this statement as having surrendered all equivalents to synthetic fiberfill. *See id.* at 1379. The Federal Circuit disagreed, reasoning that “[t]he argument . . . does not address or even relate to the composition of the fiberfill batting.”:

Rather, it was based on the '297 patent not teaching or suggesting the overall composition of materials, or the use of the disclosed compress to cool a person through evaporation. . . .

The arguments made during prosecution, and the corresponding addition of the claim limitation “by evaporation,” indicate that AquaTex was distinguishing *the overall method of cooling of its claimed invention from that of the ‘297 patent*. The subject matter surrendered by the narrowing amendment bears no relation to the composition of the fiberfill batting material. There is no indication in the prosecution history whether or not AquaTex agreed or disagreed with the examiner’s statement that the fiberfill found in the prior art comprised natural fibers. Thus, the trial court erred in holding that prosecution history estoppel barred AquaTex from asserting infringement under the doctrine of equivalents.

Id. at 1383 (emphasis added).

Illumina’s suggestion that Affymetrix surrendered any use of “tags” or “enzymes” when it amended its claims ignores the context in which those statements were made. Indeed, Affymetrix no more surrendered “tags” or “enzymes” than it did “DNA” in the course of distinguishing the Weiss and Stockham references.

Illumina emphasizes Affymetrix’s statement to the Examiner that its invention was “in stark contrast” to Weiss and Stockham. The basis for the “stark contrast,” however, was not that enzymes and tags were used in Weiss or Stockham (as they are in many molecular biology applications), but rather the fact that Weiss utilizes identical probes (which bind to identical tags), and both references involve the visualization and analysis of sequencing ladders, whereas Affymetrix’s invention analyzed signals generated by probes differing by at least a

single base. (See DTX 4, IAFP00000401-404 (May 20, 1996 Amendment)). Indeed, there are no “tags” used in Stockham, and the “enzyme” mentioned in Weiss is used to visualize a fluorescent substrate. (*Id.* at IAFP00000402-403). By contrast, Illumina’s assays utilize an enzyme to assist in distinguishing the extent of hybridization of a perfect match and a single-base mismatch, a completely different use of enzymes than found in Weiss and Stockham.

Affymetrix distinguished Weiss on the basis that all probes were identical and bound to identical tags to visualize the sequencing ladder, Stockham on the basis that it used no probes and no fluorescent signal, and both references as involving sequencing utilizing a sequencing ladder – not array-based sequencing in which an intensity from a probe location indicated the extent of hybridization of a probe and sample sequence. (*See id.* at IAFP00000402-403). Affymetrix argued that Weiss involved a single probe sequence, not a plurality, and involved sequencing using nucleic acid ladders.

Weiss **uses a single probe** which will hybridize to a tag on the nucleic acid ladder fragments. As such, **all of the “probes” in Weiss are identical**. Furthermore, the probes in Weiss do not indicate an extent of hybridization but instead are utilized to generate a fluorescent signal which indicates the location of a fragment on the substrate. Accordingly, **it is the location of the fragments that is used to sequence a nucleic acid**.

(*Id.* (emphasis added)). Affymetrix argued that Stockham included *no probes*, at all, and, again, represented ladder-based sequencing:

Stockham does not utilize probes at all. Instead, Stockham recites that the fragments of the nucleic acid ladder are radioactively labeled. The radioactive signal resulting indicates the position of the fragments in the gel in a way which is similar to Weiss. Accordingly, **Stockham also utilizes the location of the fragments to sequence a nucleic acid**.

(*Id.* at IAFP00000403 (emphasis added)). It was these points of distinction that stood “in stark contrast” to Affymetrix’s invention – not the use of “tags” or “enzymes”:

In stark contrast, the present invention compares probe intensities that indicate the extent of hybridization of probes differing by a single base. . . .

(*Id.*).

Affymetrix made this point again later in its remarks, stating that “Weiss and Stockham relate to vastly different technologies than the pioneering advances of Fodor” because “Weiss and Stockham are directed to identifying the location of a fragment of a nucleic acid ladder,” in contrast to Affymetrix’s invention, which involved signals from an array associated with hybridization events. (*Id.* (emphasis original)).

Thus, the prosecution history makes clear that Affymetrix did not “clearly and unmistakably surrender” the use of enzymes and tags in assays like those of Illumina. To the contrary, Affymetrix distinguished Weiss and Stockham on completely different grounds. Illumina’s attempt to transform Affymetrix’s prosecution arguments to support its estoppel theory has no basis in law or the facts of the prosecution.

CONCLUSION

For the foregoing reasons, Illumina’s Motion To Vacate As A Matter Of Law The Jury’s Verdict Of Infringement Of The ‘716 Patent Should Be **DENIED**.

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